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EXAMINER
FOX, DAVID T

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12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/886,207	Applicant(s) Keller et al
	Examiner Fox	Group Art Unit 1638

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE - 3 - MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 12/19/02.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 59-74 and 76-99 is/are pending in the application.

Of the above claim(s) 77-79, 85-87 and 93-95 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 59-74, 76, 80-84, 88-92, 96-99 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☑ Information Disclosur Statement(s), PTO-1449, Paper No(s). 7

☐ Intervi w Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

Applicant's election with traverse of Group I in Paper No. 11 is acknowledged. The traversal is on the ground(s) that all claims depend upon those of Group I, and that the search for Group I would encompass the other groups. This is not found persuasive regarding Group II because Group II requires particular *Brassica* plants with particular transgenes and particular phenotypes, all not required by Group I, thus requiring a separate search. As admitted by Applicants in the paragraph bridging pages 11 and 12 of the specification, *Brassica* has been traditionally recalcitrant to transformation, thus requiring particular transformation methods and regeneration methods requiring a separate search. Furthermore, as admitted by Applicants on page 13 of the specification, bottom paragraph, the particular *Brassica* genotype of claims 78-79, 86-87 and 94-95 requires specialized transformation and regeneration methods, each requiring a separate search. Applicants' arguments regarding Group III are persuasive, and Groups I and III have been rejoined.

The requirement is still deemed proper and is therefore made FINAL.

Claims 59-74, 76, 80-84, 88-92 and 96-99 are examined in the Office action that follows.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 69-70, 83-84, 88-92 and 96-98 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 69-70 are indefinite in their recitation of "said particular plant" which lacks antecedent basis in claim 59. Deletion of "particular" would obviate this rejection.

Claims 83, 88 and dependents are indefinite in their recitation of "or a related derivative" as the degree of relatedness or structural similarity is unclear. Deletion of the phrase would obviate this rejection.

Claim 91 is indefinite in its recitation of "the auxin transport inhibitor" which lacks antecedent basis in claim 88. Amendment of claim 91 to depend upon claim 89 would obviate this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59-67, 69-74, 76, 80--84, 88-92 and 96-99 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a genetic construct comprising any conditionally lethal gene of any sequence and from any organism, including "oncogene 2" of any sequence and from any organism. Claim 71 is broadly drawn to the use of any promoter of any sequence from any low termperature-inducible gene from *Arabidopsis*; as well as three other conditional lethal genes from any organism and of any sequence including genes encoding methoxinine dehydrogenase,

rhizobitoxine synthase, and phosphonate monester hydrolase. The claims are also drawn to transformed plant cells and plants containing those genetic constructs, and methods of use of the genetic constructs.

In contrast, the specification only provides guidance for a genetic construct comprising the oncogene 2 coding sequence from *Agrobacterium tumefaciens* under the control of a constitutive CaMV 35S promoter. No guidance is provided regarding the identification, isolation or characterization of any other conditionally lethal gene from any species and of any sequence, any other "oncogene 2" from any species and of any sequence, any promoter of any sequence from any low temperature-inducible *Arabidopsis* gene, or any gene of any sequence and from any organism encoding the above three enzymes.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California* v. *Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." *Id.* Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." *Id.*

See MPEP Section 2163, page 156 of Chapter 2100 of the August 2001 version, column 2, bottom paragraph, where it is taught that

[T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus of sequences as broadly claimed. Given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming plant cells and plants therewith, and the resultant products including the claimed transformed plant cells and plants containing the genus of sequences, would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time of filing. See the Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111).

See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene (which includes a promoter) is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

See also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and

the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

Claims 59-67, 69-74, 76, 80-84, 88-92, and 96-99 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to a genetic construct comprising the Agrobacterium tumefaciens oncogene 2 coding region, does not reasonably provide enablement for claims broadly drawn to a genetic construct comprising any conditional lethal gene including any "oncogene 2" from any species and of any sequence, any gene encoding any of the three enzymes recited in claim 71, or any promoter from any Arabidopsis gene which is induced by low temperature. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a genetic construct comprising any conditionally lethal gene of any sequence and from any organism, including "oncogene 2" of any sequence and from any organism. Claim 71 is broadly drawn to the use of any promoter of any sequence from any low termperature-inducible gene from *Arabidopsis*; as well as three other conditional lethal genes from any organism and of any sequence including genes encoding methoxinine dehydrogenase, rhizobitoxine synthase, and phosphonate monester hydrolase. The claims are also drawn to transformed plant cells and plants containing those genetic constructs, and methods of use of the genetic constructs.

In contrast, the specification only provides guidance for a genetic construct comprising the oncogene 2 coding sequence from *Agrobacterium tumefaciens* under the control of a constitutive CaMV 35S promoter. No guidance is provided regarding the identification, isolation or characterization of any other conditionally lethal gene from any species and of any sequence, any other "oncogene 2" from any species and of any sequence, any promoter of any sequence from any low temperature-inducible *Arabidopsis* gene, or any gene of any sequence and from any organism encoding the above three enzymes. In addition, no guidance is provided regarding the evaluation of any non-exemplified gene construct for its ability to cause a reversible or sub-lethal conditional lethal phenotype.

The use of oncogenes to cause a conditional lethal phenotype is unpredictable. Smigocki et al teach that plant transformation with a genetic construct comprising the *Agrobacterium tumefaciens* oncogene 4 sequence (*ipt* gene) ligated to a strong constitutive promoter resulted in increased shooting and cell culture proliferation (see, e.g., page 5131, Abstract), rather than any type of lethality. Medford et al teach that the expression of a genetic construct comprising a heat-inducible heat shock promoter ligated to the *ipt* gene unpredictably did not change whether or not the heat shock promoter was actually induced (see, e.g., page 403, Abstract).

The use of topical plant application of chemicals to induce conditionally lethal genes is unpredictable. See, e.g., Kriete et al, page 815, column 1, to paragraph, who teach that most chemicals which are allegedly non-toxic precursors of toxins either are in fact phytotoxic or do not persist in the field environment, wherein the precursors when applied to plants transgenic for

an enzyme-encoding gene are able to be converted into the toxic form, thus effecting a conditional lethal phenotype. See also the instant specification, page 14, bottom paragraph; page 15, top paragraph; page 28, middle paragraph; where it is taught that most chemically-activatable conditional lethal genes have the disadvantage that they lead to cell death and plant lethality, thus preventing the recovery of a desired plant for further breeding, and that the *Agrobacterium tumefaciens* oncogene 2 is unique in its ability to effect a controllable, sub-lethal phenotype.

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to identify, isolate or evaluate a multitude of non-exemplified conditionally lethal genes including non-*Agrobacterium tumefaciens* oncogene 2. Undue experimentation would have also been required to identify and isolate promoters from *Arabidopsis* low temperature-inducible genes, and to evaluate their ability to controllably and effectively cause conditional lethality in planst transformed therewith.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 59-60, 64-65, 69-70, 73-74 and 76 are rejected under 35 U.S.C. 102(b) as being anticipated by Dotson et al (U.S. Patent 5,254,801).

The claims are broadly drawn to a genetic construct comprising a coding sequence encoding a conditionally lethal gene product, ligated to a promoter which is expressible in at least one plant cell, or is expressible in response to a chemical stress, or is tissue-specific, which construct further comprises a second gene which confers a measurable change in phenotype, which encodes a protein; and are also broadly drawn to vectors and transformed plants containing the construct.

Dotson et at teach a genetic construct comprising the conditionally lethal phosphonate monoester (peh) gene under the control of a constitutive enhanced CaMV 35S promoter for expression throughout the entire plant or under the control of a tapetum-specific p127a promoter, wherein said genetic construct further comprises a kanamycin resistance gene encoding a protein which confers the measurable phenotype of antibiotic resistance to the plant cell; and also teach vectors and transformed plants comprising the construct, wherein topical application of the chemical glycerol glyphosate, which may itself be considered a chemical stressor due to its slight toxicity, allows the production of the herbicide glyphosate in the transformed plant cells which express the *peh* gene (see, e.g., columns 1, 2, 4, 5, 7-9, 22-24 and 27-31; Figures 8-10).

Claims 59-60, 64-65, 67-70, 74, 76 and 80-84 are rejected under 35 U.S.C. 102(b) as being anticipated by Jorgensen (U.S. Patent 5,278,057).

Claims 67-68 and 80-84 are drawn to a genetic construct comprising the *Agrobacterium tumefaciens* oncogene 2 (or *iamH* gene encoding indoleacetamide hydrolase) as the conditionally lethal gene and further comprising a second gene encoding a protein conferring another selectable

and measurable phenotype, and methods for activating a conditionally lethal phenotype comprising topical application of an indoleamide (including naphthalene acetamide or NAM) of a plant which has been transformed with the construct, wherein the expression of the oncogene 2 in all cells of the plant is sufficient to cause lethality in every cell in which it is expressed.

Jorgensen teaches a genetic construct comprising oncogene 2 under the control of a constitutive promoter and further comprising a kanamycin resistance gene, and methods for plant transformation therewith and activation of the condtionally lethal (or sub-lethal) phenotype by topical application with naphthalene acetamide, wherein visual symptoms of conditional lethality or sublethality including epinasty and leafroll were observed (see, e.g., columns 23-27).

Claims 59-60, 64-70, 72-74 and 76 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/40179 (PIONEER).

Claim 66 is drawn to a construct which comprises a second gene conferring an input trait (defined in the instant specification on page 2 as including herbicide resistance). Claim 72 is drawn to a genetic construct comprising an inducible promoter ligated to the conditionally lethal gene.

PIONEER teaches a genetic construct comprising the *iamH* gene ligated to a seed-specific promoter such as the phaseolin or napin promoters, the pollen-specific *Brassica* L4 ("Bp 4") promoter, the heat- or light- or chemical-inducible heat shock, GST II, or CAB promoters, respectively; said genetic construct further comprising a PAT gene conferring resistance to the

herbicide bialaphos; vectors and plants transformed therewith (see, e.g., columns 9, 12-15 and 19-21).

Claims 59-60, 64-70, 72-74, 76 and 80-84 are rejected under 35 U.S.C. 102(b) as being anticipated by Fabijanski et al (U.S. Patent 5,426,041).

Fabijanski et al teach a genetic construct comprising oncogene 2 under the control of a constitutive promoter or pollen-specific L4 promoter or inducible promoter, and further comprising a kanamycin resistance gene, and methods for plant transformation therewith and activation of the condtionally lethal (or sub-lethal) phenotype by topical application with naphthalene acetamide (see, e.g., columns 5-9, 15-20, 25-27 and claims 1-6).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 59-60, 64-65, 69-74, 76 and 80-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dotson et al (U.S. Patent 5,254,801).

Claims 69 and 72 are drawn to the use of a chemically inducible promoter ligated to the conditionally lethal gene. Claims 80-82 are drawn to the use of a conditionally lethal gene to remove a plant from the environment.

The teachings of Dotson et al have been discussed *supra*.

Dotson et al do not explicitly teach a chemically inducible promoter or the use of the conditionally lethal gene to remove a whole plant from the environment.

Dotson suggest the use of inducible promoters, and the use of the conditionally lethal gene to remove undesired individuals, and also teach the use of the conditionally lethal gene as a selection means for cells cultured on a medium containing a chemical which is converted into a toxic substance by the product of the conditionally lethal gene expressed under the control of the constitutive enhanced CaMV 35S (see, e.g., column 5, lines 13-25; column 9, lines 20-23; column 29, line 11 through column 30, line 47).

It would have been obvious to one of ordinary skill in the art to utilize the genetic construct comprising a conditionally lethal gene as taught by Dotson et al, and to modify that construct by incorporating an inducible promoter such as an available chemically inducible promoter, given the suggestion to do so by the reference and the recognition by those of ordinary skill in the art that choice of type of available inducible promoter would have been the optimization of process parameters. It would have also been obvious to utilize the conditionally

lethal gene as a negative selection marker for a whole plant, as suggested by Dotson et al, given the recognition by those of ordinary skill in the art of the ecological advantages of eliminating superfluous transgenic plants from the environment, and given the recognition that the constitutive promoter utilized by Dotson et al would function in all cells of a whole plant.

Claims 61-63 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dotson et al (U.S. Patent 5,254,801) in view of Goodman et al (U.S. Patent 5,550,038).

The claims are drawn to the use of a genetic construct comprising a conditionally lethal gene and another gene encoding an output trait such as the production of a pharmaceutically active compound or an industrial enzyme.

Dotson et al teach the use of a conditionally lethal gene as a marker gene or as a way to rogue transformed plants from the environment once they are no longer needed, as discussed above, but do not teach the use of plants as bioreactors.

Goodman et al teach the advantages of using plant cells and plants as bioreactors for producing a multitude of pharmaceutically active compounds or industrial enzymes, as exemplified by the production of interferon which is correctly folded and glycosylated, and also teach the advantages of using a selectable marker gene to identify transformed plant cells (see, e.g., column 1, lines 12-49; column 2, lines 1-12; column 3, line 12 through column 4, line 9; column 5, line 55 through column 10, line 23).

It would have been obvious to one of ordinary skill in the art to utilize the method of plant transformation with a conditionally lethal gene and a second gene as taught by Dotson et al, and

to modify that method by incorporating a gene encoding a pharmaceutical or an industrial enzyme, as suggested by Goodman et al.

Claims 88, 92 and 96-98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fabijanski et al (U.S. Patent 5,426,041) in view of Dotson et al (U.S. Patent 5,254,801).

The claims are drawn to the use of the *Agrobacterium tumefaciens* oncogene 2 conditionally lethal gene as a marker gene for identifying transformed seeds or embryos.

Fabijanski et al teach plant transformation with *Agrobacterium tumefaciens* oncogene 2, as discussed above, but do not teach the use of the gene as a selectable marker for transformed seeds or embryos.

Fabijanski et al also teach the use of the oncogene 2 as a selectable marker gene for transformed pollen grains cultured on a medium containing the substrate of the enzyme (see, e.g., column 29, line 30 through column 30, line 57).

Dotson et al teach the use of a conditionally lethal gene as a marker, as discussed above.

It would have been obvious to one of ordinary skill in the art to utilize the genetic construct comprising the *Agrobacterium tumefaciens* oncogene 2 taught by Fabijanski et al as a selectable marker, as suggested by Dotson et al. Furthermore, it would have been obvious to utilize the seed or embryo tissue as the tissue to be assayed, given the successful teaching of Fabijanski et al of the use of the oncogene 2 as a marker gene in other plant organs, and given the recognition by those of ordinary skill in the art that choice of explant or tissue type to be assayed for transformation would have been the optimization of process paramters.

Claims 71, 89-91 and 99 are deemed free of the prior art, given the failure of the prior art to teach or suggest an isolated cold-activatable promoter from *Arabidopsis*, or the use of an auxin transport inhibitor in a selection medium for obtaining whole transformed plants which comprise oncogene 2 from *Agrobacterium tumefaciens*.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is (703) 308-0280. The examiner can normally be reached on Monday through Friday from 10:30AM to 7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (703) 306-3218. The fax phone number for this Group is (703) 872-9306. The after final fax phone number is (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

March 10, 2003

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638